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(54) **Antimicrobial quaternary ammonium group-containing polymers, compositions thereof, and monomers used to produce said polymers**

Quaternäre Ammoniumgruppen-enthaltende antimikrobielle Polymere, Zusammensetzungen auf Basis dieser Polymere und Monomere für ihre Herstellung

Polymères antimicrobiens contenant des groupes d'ammonium quaternaire, compositions à base de ces polymères et monomères pour leur préparation

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Description

This invention relates to quaternary ammonium group-containing organosilicon polymers and novel monomers used to produce these polymers. The invention also relates to methods of producing such polymers and monomers. The polymers may be used in wide applications as antimicrobial agents as, for example, in solutions to disinfect contact lenses and certain of these polymers may be used to produce solid structures, such as contact lenses.

Contact lenses are typically made of hydrophilic and partially hydrophilic plastic materials. These materials have a high capacity to absorb water and swell to a soft mass or hydrogel. This hydrogel is characterized by excellent mechanical properties, complete transparency, good shape retention and high resistance to degradation in boiling water. Such hydrophilic or partially hydrophilic plastic materials are described in such patents as US-A-2,976,576, US-A-3,499,862 and US-A-3,503,942. These patents disclose, inter alia, the production of the so-called soft contact lenses.

One of the problems associated with cleaning soft contact lenses made from the aforementioned hydrophilic materials, is in the disinfecting and cleaning of such lenses. These lenses have a high capacity to absorb water, i.e. upwards of about 38 weight % water, based on the total weight of the hydrogel. Therefore, the compounds employed to disinfect the contact lenses are often absorbed and possibly even concentrated in the lenses and later released when the soft contact lenses are worn on the eye. This, of course, may damage or stain the contact lenses and harm the sensitive tissues of the eye. Such preservative or disinfectant materials typically used to disinfect the contact lenses may be such materials as chlorohexidine or thimerosal, for example.

To overcome these problems, materials such as quaternary ammonium group-containing polymers having antimicrobial activity may be used to disinfect the lenses. The advantage of using antimicrobial polymers is that they have a larger molecular size and are less likely to penetrate or be absorbed into the soft contact lenses, and tend to be less toxic.

Examples of such polmyers are the polymeric quaternary ammonium compounds having recurring vinyl benzene ammonium units. Such polymers are disclosed in US-A-4,482,680. These polymers have a disadvantage in that they have relatively poor solubility in water.

Another example of polymers employed for disinfecting contact lenses are the organosilicon quaternary ammonium compounds disclosed in US-A-4,615,882. These polymers are produced by reacting an organosilicon quaternary ammonium salt having a hydrolyzable group with a water soluble high molecular weight organic polymer, such as polyvinyl alcohol, reactive with said hydrolyzable group. The hydrophilic polymers described in US-A-4,615,882 have silicone and quaternary ammonium components as required in the present invention, however the synthesis of the polymers disclosed in the patent result in the formation of hydrolytically unstable linkages, e.g. silicon-oxygen-carbon linkages. Such Si-O-C bonds are unstable, break down over time, and the existence of such bonds could lead to toxicity problems.

The present invention relates to quaternary ammonium group-containing organosilicon polymers having antimicrobial activity which do not have the unstable linkages, i.e. the silicon-oxygen-carbon linkages of US-A-4,615,882 and therefore are free of the toxicity problems due to the breakdown of these compounds with time.

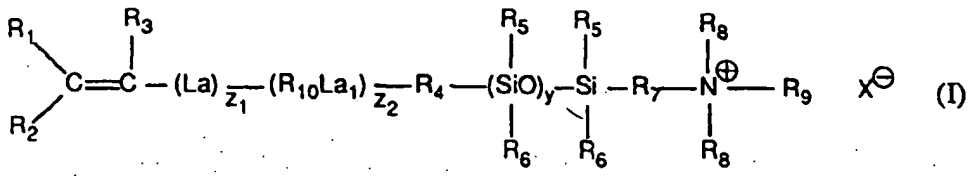
The antimicrobial polymers of the present invention are suitable for treating soft contact lenses and are especially suitable for cleaning and disinfecting such lenses to remove proteinaceous deposits which tend to form and build on the lenses during wear and handling.

The polymers of the present invention are of such a molecular size that they do not penetrate the contact lenses polymer matrix as readily as non-polymeric organic molecules, and when they do penetrate, are less toxic than said non-polymeric compounds. Therefore, they are less apt to damage the lenses or injure the eye as is typical of non-polmyeric materials which penetrate the lenses and may leach out and damage the soft tissues of the eye during the use thereof.

The organosilicon quaternary ammonium compounds of the present invention may typically be dissolved or dispersed in a solution, especially an aqueous solution, used to disinfect the contact lenses and are used in amounts sufficient to disinfect the lenses. The polymers of the present invention have advantages over the poly(vinylbenzyl quaternary ammonium) halide structure disclosed in the Sheldon patent, US-A-4,482,680, in that they are more water soluble and therefore can be more easily dissolved in aqueous solutions. The solutions, according to the present invention, are preferably aqueous based solutions, occasionally containing organic solvents, which are nontoxic to the eye, i.e. are ophthalmically safe for use.

Although the quaternary ammonium-containing organosilicon compounds of the present invention are especially suitable for disinfecting soft lenses, they can also be used for other utilities where the antimicrobial properties are effective, i.e. for hair care and in other topical pharmaceutical products. Specific uses may be in the therapeutic skin care preparations and us as deodorants or antimicrobials for the body. In addition, the products can be formulated with various cleanser components to form disinfectants for home or hospital use.

The quaternary ammonium group-containing organosilicon polymers of the present invention can be produced by homo- or copolymerizing a monomer of the following generic structure of formula I



(I)

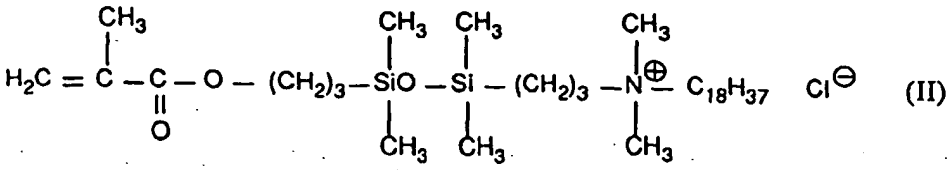
wherein R_1, R_2 and R_3 are independently hydrogen, C_1-C_7 alkyl, or -$COOR_{13}$ with R_{13} being hydrogen or C_1-C_4 alkyl;
z_1 and z_2 are independently 0 or 1;
La is -C(O)O-, -C(O)N(R_a)-, or a bond;
La_1 is a bond, -C(O)O-, -C(O)N(R_a)-, -O-, -OC(O)O-, -N(R_a)C(O)N(R_a)- or -N(R_a)C(O)O-;
wherein R_a is hydrogen or C_1-C_8 alkyl;
R_{10} is a bivalent C_1-C_{20} aliphatic, C_3-C_{25} cycloaliphatic or C_6-C_{20} aryl group, each of which may be substituted with up to five halogen atoms, or $(CH_2CH(R_a)O)_j$, wherein j is an integer from 1 to 50 and R_a is as defined hereinbefore;
R_4 and R_7 are independently a bivalent group selected from C_2-C_{10} aliphatic, such as C_2-C_8 alkylene, C_1-C_4 alkylene-(oxy-C_1-C_4 alkylene)$_g$, C_1-C_4 alkylene-OCH_2-(hydroxy C_1-C_4 alkylene)-CH_2, cycloaliphatic up to 25 carbon atoms and aryl up to 25 carbon atoms, wherein g is an integer from 1 to 10;
y is an integer from 1 to 10;
R_5 and R_6 are independently C_1-C_8 alkyl, C_6-C_{25} aryl, or C_6-C_{25} cycloaliphatic which may be substituted by one or more halogen, hydroxy, C_1-C_4 alkyl, carboxy or C_1-C_{12} perhaloalkyl groups, or R_5 and R_6 may be -$Si(OSiCH_3)_3$;
R_8 and R_9 are independently C_1-C_{24} alkyl, C_3-C_{24} cycloaliphatic or C_6-C_{25} aryl, which groups may be each substituted with from 1 to 11 groups selected from hydroxy, C_1-C_4 alkyl, carboxy, C_1-C_{12} perhaloalkyl, and halogen, or R_8 and R_9 may also be $(CH_2CH_2O)_xH$ units, where x is an integer from 1 to 10, and
X is an ophthalmically acceptable counterion.

The ophthalmically acceptable counterion X is preferably a halogen, hydroxy, acetate, SO_4^{2-}, CO_3^{2-}, or PO_4^{3-} for example. If not otherwise defined, a bivalent C_1-C_{20} aliphatic group is preferably C_1-C_{10} alkylene, more preferred C_1-C_6 alkylene. Likewise, the cycloaliphatic groups are all preferably groups having 3 to 25 carbon atoms, more preferred cycloalkyl groups containing 6 to 10 carbon atoms, and more preferably 5 to 7 membered cycloaliphatic groups, including e.g. combinations of cycloalkyl and lower alkyl. A preferred cycloalkyl is cyclohexyl. Likewise, aryl groups preferably have 6 to 25 carbon atoms, more preferred 6 to 10 carbon atoms. A preferred aryl group is phenyl. Halogen is e.g. fluoro, chloro or bromo, of which fluoro and chloro are preferred.

Preferred are those monomers of formula I wherein R_1, R_2 and R_3 are independently hydrogen or C_1-C_4 alkyl;

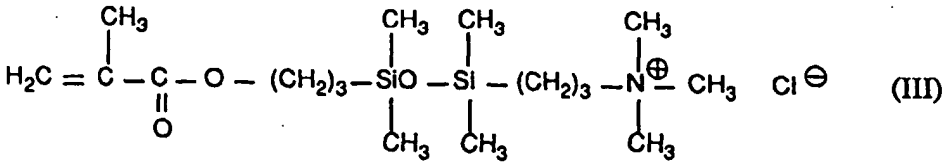
z_1 and z_2 are independently 0 or 1;
La is -C(O)O- or a bond;
La_1 is a bond, -N(R_a)C(O)N(R_a)- or -N(R_a)C(O)O-;
wherein R_a is hydrogen or C_1-C_4 alkyl;
R_{10} is a bivalent C_1-C_6 alkylene, or phenyl group,
R_4 and R_7 are independently a bivalent C_2-C_6 alkylene;
y is an integer from 1 to 10, preferably 1 to 5;
R_5 and R_6 are independently C_1-C_4 alkyl;
R_8 and R_9 are independently C_1-C_{24} alkyl, and
X is an ophthalmically acceptable counterion.

Typical and preferred structures of the above monomers have the following formulae:

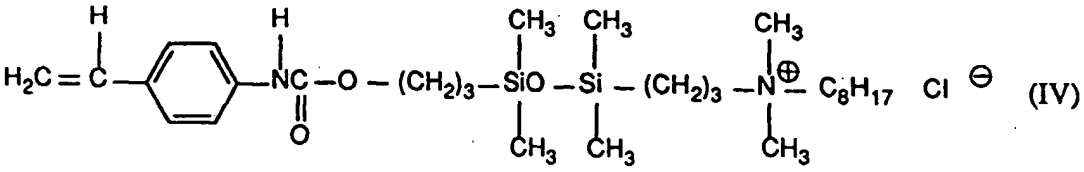


(II)

3-methacryloxypropyltetramethyldisiloxanylpropyldimethyloctadecylammonium chloride (MADAC),



(III)



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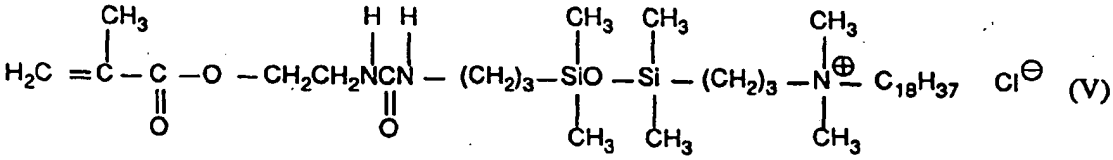
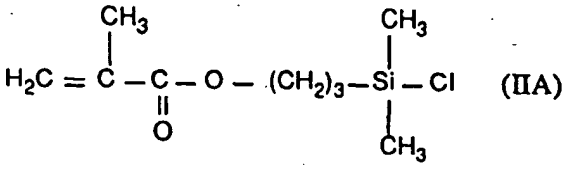


(V)

The novel monomers of the present invention used to produce the organosilicon polymers are a further embodiment of this invention. A description of a typical procedure for producing these novel monomers is reproduced hereinafter. Below is a synthetic scheme for the production of the MADAC monomer of the formula II (a typical and preferred monomer) used in producing the water soluble polymers and contact lens materials of the present invention.

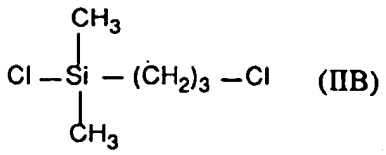
Step 1

A compound of the formula IIA



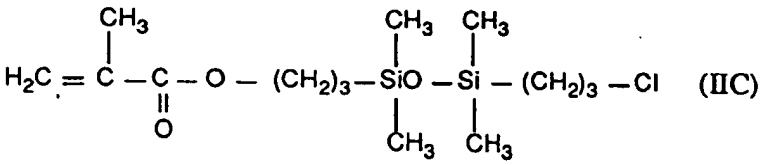
(IIA)

is r acted with a compound of the formula IIB



(IIB)

in the presence of water to produce a compound of the formula IIC

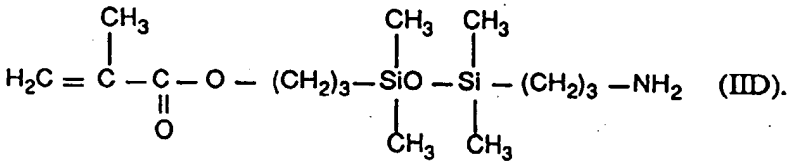


(IIC)

and HCl as a by-product.

Step 2

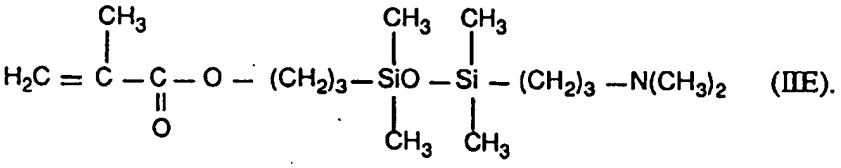
The compound of the formula (IIC) is reacted with an excess of NH_3, to produce a compound of the formula IID



(IID).

Step 3

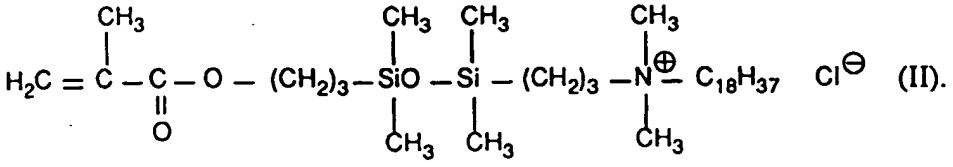
Said compound of the formula IID is reacted with an excess of CH_3Br to produce a compound of the formula IIE



(IIE).

Step 4

The compound of the formula IIE is quaternized with $C_{18}H_{37}Cl$ to produce a compound of formula II (MADAC)



(II).

The reaction conditions in Step 1 may be varied, but it is usually carried out preferably from about ambient temperatures to about 40°C in an aqueous solution, which may be slightly acidic.

The reaction with the amine in Step 2 is preferably carried out in an aqueous solution at a temperature from about 0°C to about ambient temperature and preferably from about 0°C to about 20°C. This reaction is ordinarily carried out at atmospheric pressure, however, it can be carried out under high pressure at even higher temperatures, if necessary.

Step 3 is preferably carried out at a reaction temperature of from about room temperature to up to about 40°C in a suitable organic solvent, especially an inert organic solvent, such as toluene and benzene.

Step 4 may be carried out in a solvent, preferably at room or ambient temperature. The solvents include such organic solvents as toluene, benzene and other inert, typically used solvents. The reaction conditions vary depending upon the nature of the reactants, solvents employed and pressure conditions. The above conditions represent the typical conditions employed.

The other monomers of the generic formula (I) can be produced by following the same reaction scheme used to produce the MADAC monomer as set forth in Steps (1) to (4) above.

The quaternized monomers of the generic formula (I) set forth above, may be homo- or co-polymerized to produce the final polymer structure. The monomers are typically polymerized in an inert atmosphere, such as nitrogen or argon, free of oxygen. The polymerization may be initiated by way of initiators, such as peroxides or azobisisobutyronitrile (AIBN) in amounts sufficient to initiate the reaction, i.e. typically from about 0.01 to 0.5 weight % based on the weight of the monomer. The reaction may be carried out in the presence of a solvent, such as an alcohol, toluene, benzene, tetrahydrofuran or a ketone, such as methylethyl ketone. The reaction may be carried out by heating the reaction solution at elevated temperatures and preferably at temperatures from about 40°C to about 150°C or the reflux temperature of the solvent. The temperature varies depending upon the monomers and other materials present in the reaction solution.

The reaction may also be carried out by subjecting the reaction solution to a UV source to produce the final product. The reaction is carried out for a time sufficient to complete the polymerization, which reaction may proceed for time periods up to about 100 hours or more. The initiator used in the polymerization reaction is dependent upon the type of energy source used and may be different if a UV source is used as opposed to a thermal energy source.

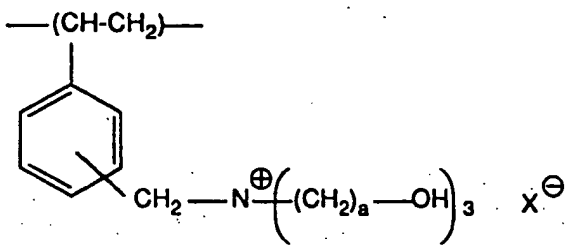
The above monomers of formula (I) may be homopolymerized or they may be copolymerized with suitable comonomers. This copolymerization reaction thus includes the reaction of the quaternary ammonium group-containing organosilicon monomers with one or more comonomers.

The copolymers may contain copolymeric units having a generic structure depicted as -M-. The copolymeric units can be added to achieve the desired physical properties, enhance the solubility in aqueous or nonaqueous media, achieve better miscibility in various solvents or to improve the dispersibility of the polymer.

The first type of M units is represented by vinylaromatics, e.g. styrene, lower alkenes or lower alkadienes, such as ethylene, butadiene and the like. The second type of M units is illustrated by vinyl acetamide, vinyl amines, vinyl amine quaternized with hydroxyethylenes or similar water solubilizers or with hydrophobes such as alkyls, e.g. dodecyls, or vinylbenzyl amine quaternized with three long chain alkyl hydrophobes or with three lower alkyl or hydroxyalkyl hydrophiles. Other units include, for example, vinyl acetate, vinyl alcohol, acrylic acid, acrylate and methacrylate esters; acrylamide and acrylamide derivatives, including quaternized acrylamide; N-vinylimidazole and derivatives thereof, including quaternized N-vinylimidazoles; 4-vinylpyridine and derivatives thereof, including quaternized 4-vinylpyridines; N-vinylpyrrolidone and derivatives thereof; vinylbenzyl ethers of polyethylene glycols and their monoalkyl ethers. These units are all known in the art as are the methods for their incorporation into copolymers. Mixtures of two or more M units may, of course, be used. The term "lower" used in the context of this invention defines radicals or groups having preferably up to 7 carbon atoms, more preferred up to 4 carbon atoms.

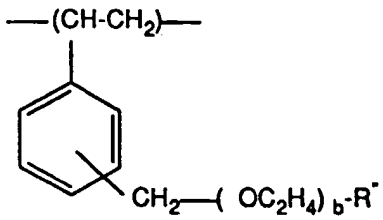
Generically, the M units can be grouped as 2 to 6 carbon alkylenes or alkenylenes, having pendent therefrom, from 0 to 2 substituent groups selected from aryls, alkaryls, and aralkyls of 6-8 carbons, alkyls of 1-4 carbons, amides, hydroxyls, carboxylic acids, and their esters, preferably lower alkyl esters, nitrogen-containing 5 or 6 atom heterocyclics and amine and ether-substituted aryls, alkaryls and aralkyls.

The M copolymer units may be vinylbenzyl amines quaternized by hydrophilic groups such as hydroxyalkyls of from 1 to 4 carbon atoms, particularly vinylbenzyl amines quaternized with three 2-hydroxyethylenes (i.e. with a triethanolamine structure). Such units are represented structurally as



wherein a is 2 through 4 inclusive and most preferably 2.

Another group of copolymer units M contemplated herein are vinylbenzyl ethers of poly(ethylene glycol)s or their mono-lower alkyl ethers, particularly methyl ethers. Such units are represented structurally as



wherein b is 1 through 10 inclusive, preferably 1 through 4 inclusive, and R" is hydroxy or lower alkoxy, such as alkoxy having from 1 to 4 carbons, e.g. methoxy, ethoxy, propoxy or butoxy, most generally methoxy.

As can be seen from the above, any compatible copolymer unit can be polymerized with the monomers (I) to incorporate the antimicrobial quaternary group-containing organosilicon monomers (I) of the present invention into the polymer structure as long as the monomers do not deleteriously affect the objective purposes of the present invention, which is primarily to achieve antimicrobial effects, for disinfecting contact lenses.

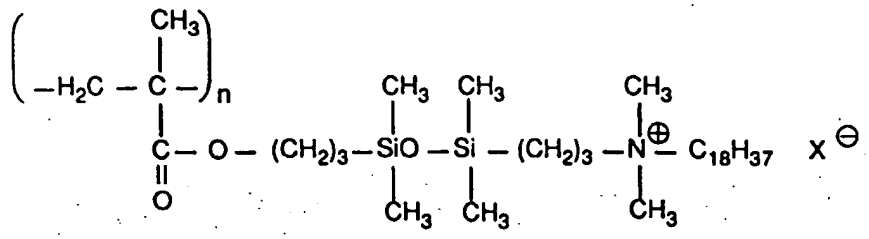
The polymers of the present invention may be crosslinked with various crosslinking agents. Examples of such crosslinking agents are allyl compounds e.g. allyl methacrylate, diallyl itaconate, monoallyl itaconate, diallyl maleate, diallyl fumarate, diallyl succinate, diallyl phthalate, triallyl cyanurate, triallyl isocyanurate, diethylene glycol bis-allyl carbonate, triallyl phosphate, triallyl trimellitate, allyl vinyl ether, N,N-diallylmelamine; vinyl compounds, e.g. divinyl benzene, N,N'-methylene bis acrylamide, ethylene glycol dimethacrylate, neopentylglycol dimethacrylate, tetraethylene glycol dimethacrylate, hexamethylene bis maleimide, divinyl urea, bisphenol A bis methacrylate, divinyl adipate, glycerin trimethacrylate, trimethylolpropane triacrylate, trivinyl trimellitate, 1,5-pentadiene, 1,3-bis(4-methacryloxybutyl) tetramethyl disiloxane, divinyl ether and divinyl sulfone; hydroxyl reactive compounds such as polyvalent isocyanates, e.g. hexamethylene diisocyanate, isophorone diisocyanate, toluene diisocyanate; polyaldehydes, e.g. glutaraldehyde and glyoxal; polyacids, e.g. glutaric acid and oxalic acid; polyepoxides, e.g. butane diepoxide, vinylcyclohexane dioxide and butanediol diglycidyl ether; polyols (acid catalysis), e.g. dimethylol urea and diethylene glycol.

The amounts of such crosslinking agents are dependent upon the purpose desired and usually about 0.01 to 10 weight % of the crosslinking agent, based upon the weight of the monomers may be used.

The polymers of the present invention preferably have average molecular weights ranging from about 2,000 to about 1,000,000 for the homo- or co-polymer. The average molecular weight as used herein means the weight average molecular weight (M_w) as determined by light scattering measurement.

The number of recurring units, i.e. the mers units, ranges from about 10 mers to about 3,000 mers for the quaternary ammonium group-containing organosilicon monomers in the homopolymers or in the case of copolymers, the total number of units of all the comonomers ranges from 10 mers to about 3,000 mers.

The homopolymer of the monomers of the present invention as represented by the polymerized MADAC monomer of Formula (II) above, is expressed by the following formula:



wherein n is an integer of 10 to about 3000 and X is an ophthalmically acceptable counterion, which is preferably Cl. As can be seen from the above, the polymerization takes place at the reactive alkene terminal portion of the MADAC monomer. The n group varies between about 10 mers up to about 3,000 mers as previously mentioned. The comonomers M, similarly react at the alkene portion of the quaternary ammonium group-containing monomer structure.

The polymerization and copolymerization methods discussed above relate to the homopolymerization or copolymerization of the quaternary ammonium group-containing organosilicon monomers, but the monomers may be homopolymerized or copolymerized before being quaternized and then subsequently quaternized. For example, the product as set forth in Step 3 (prior to the quaternizing step), may be polymerized and the resulting polymer subsequently quaternized as in Step 4 for producing the monomer as discussed above.

The polymers of the present invention are primarily used in ophthalmic solutions for cleaning lenses, particularly soft lenses, where penetration of the antimicrobial component into the soft gel structure is to be avoided. However, the liquid composition can be used on hard contact lenses and any surface where antimicrobials and preservatives are typically employed. Further, the polymers of the present invention can be used to produce contact lenses which are strong, flexible, highly oxygen permeable, wettable and optically clear.

To produce solid structures, such as contact lenses, preferably higher molecular weight polymers are employed, and especially crosslinked polymers are preferably used, which are crosslinked to a degree sufficient to attain the desirable properties as discussed above. The final lenses thus produced have sufficient antimicrobial properties to help kill bacteria and other microorganisms which grow on the lenses, but are not toxic or harmful to the eyes.

The aqueous solutions for disinfecting e.g. soft contact lenses provided herein are compatible, from pharmacological and chemical standpoints, with typical ingredients normally included in the antimicrobial or disinfectant solutions for contact lens care, and do not significantly alter the toxicity of the system. They have very low mammalian toxicity and are chemically stable, odorless and non-volatile, and exhibit a broad spectrum of anti-bacterial activity against a wide range of microorganisms which pose a danger to the eye, as exemplified by Pseudomonas aeruginosa. They are nontoxic and non-irritating to the tissues of the eye in the concentrations and frequency of use contemplated herein.

The compositions of this invention also are compatible with other ingredients usually found in ophthalmological eye care solutions. They are easily handled and applied, do not foam, and can be and are chemically stable in a wide range of pH's. However, it is preferable to apply the solutions at a pH of 7, plus or minus one unit, and in an isotonic solution, so that there will be no adverse effects to the eye from osmotic pressure due to an imbalance in the ionic strength of the solution.

In the practice of the present invention, in respect to the sterilization of contact lenses, the active quaternary ammonium group-containing organosilicon polymer is present in the solution in amounts sufficient to impart antimicrobial or disinfecting properties to the solution against pathogens, i.e. in an amount sufficient to destroy or inhibit multiplication of bacterial microorganisms such as *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa,* and *Aerobacter aerogenes,* while at the same time not causing irritation to the eye or damage to the lens.

The antimicrobial polymers of the present invention may be present in small amounts such as 0.001 weight %, based on the weight of the aqueous disinfectant solution, when used as a disinfectant to clean hard surfaces, such as contact lenses. The upper limit is dictated by factors which may cause eye irritation over long periods of time and/or damage to the soft contact lenses, when used for that purpose. An upper limit is e.g. about 0.5 weight %, but a practical range is from about 0.002 weight percent to about 0.1 weight %, based upon the weight of the aqueous disinfectant solution.

A typical disinfectant solution useful in the practice of this invention, may contain in addition to the active ingredient, buffers, stabilizers, and isotonizing agents. These additional materials should be non-toxic and should not distort or otherwise damage the contact lens and they should not lower or raise the pH below 5.5 or above 8.5 sinc this can have an adverse effect on ocular tissue.

Other disinfectants can be us d in the disinf ctant composition to nhance the sterilizing or disinfecting effects, if desir d.

The disinfectant liquid compositions of the present invention can be us d in a variety of compositions wher the

antimicrobial effects of the polymer are desired. The description of the utilities in the specification and claims should therefore not be construed as precluding the utility of such compositions or polymers in areas or fields of uses other than specifically described herein.

The following examples are given by illustration only and are not designed to limit the essential inventive concept as broadly disclosed her in. Temp rature are given in degrees Celsius. Th first thr e examples will illustrat concrete proc dures for producing the antimicrobial polymers of the present invention.

Example 1 :

To a dry, 250 milliliter, three-neck flask equipped with a condenser, nitrogen inlet and magnetic stirrer, are added 10.02 g of 50% 3-methacryloxypropyltetramethyldisiloxanylpropyl-dimethyloctadecylammonium chloride (MADAC) in methanol, 5.01 g N,N-dimethylacrylamide, 0.10 g 2-hydroxy-2-methyl-1-phenyl-propan-1-one and 100 ml methanol. The mixture is stirred and purged five minutes with nitrogen. The outlets are then sealed and the reaction system is subjected to ultraviolet light at ambient temperature for 96 hours. At the end of 96 hours the methanol is removed via rotary evaporation. The residue is purified by stirring in 200 ml hexanes for 18 hours. The resulting solids are filtered and the purification process is repeated two more times.

Example 2 :

To a dry, 250 milliliter, three-neck, water-jacketed flask equipped with a condenser, nitrogen inlet, magnetic stirrer and constant-temperature water circulator, are added 10.02 g of 50% 3-methacryloxypropyltetramethyl-disiloxanylpropyldimethyloctadecylammonium chloride (MADAC) in methanol, 5.06 g N,N-dimethylacrylamide, 0.12 g Vazo 52 (pentanenitrile-2,4-dimethyl-2,2-azobis) and 100 ml methanol. The mixture is stirred and purged five minutes with nitrogen. The outlets are then sealed and the reaction system is heated to 60°C for 96 hours. At the end of the reaction, the methanol is removed via rotary evaporation. The residue is stirred in 200 ml hexanes for 18 hours. The resulting solids are filtered and the purification process is repeated for two more times.

Example 3 :

To a dry 250 milliliter, three-neck water-jacketed flask equipped with a condenser, nitrogen inlet, magnetic stirrer and constant-temperature water circulator are added 10.03 g of 50% 3-methacryloxypropyltetramethyl-disiloxanylpropyldimethyloctadecylammonium chloride (MADAC) in methanol, 5.03 g N-vinyl pyrrolidone, 0.10 g Vazo 52 and 100 ml methanol. The mixture is stirred and purged five minutes with nitrogen. The outlets are then sealed and the reaction system is heated to 60°C for 96 hours. At the end of the reaction, the methanol is removed via rotary evaporation. The residue is stirred in 200 ml hexanes for 18 hours. The resulting solids are filtered and the purification process is repeated two more times.

The following Examples 4-6 represent examples in which the solutions of the polymers of Examples 1-3 are tested for their preservative efficacy and cytotoxicity. The formulations and results are shown in Tables 1 and 2, respectively.

Examples 4-6 :

Solutions are prepared from the polymers described in Examples 1 through 3. Table 1 indicates the concentration of each solution and solvent. Each solution is tested for preservative efficacy and cytotoxicity. The results of the microbial and toxicity tests are shown in Table 2.

Table 1

(Formulations of Examples 4-6)			
Example	**Polymer Used**	**Concentration**	**Solvent**
4	Example 1	0.025%	Saline, Isotonic
5	Example 2	0.025%	Saline, Isotonic
6	Example 3	0.025%	Saline, Isotonic

Table 2 (Cytotoxicity and Preservative Tests Results)

		Pseud monas Aeruginosa *		Aspergillus Fumigatus *	
Example	Cytotoxicity	24 Hours	7 Days	24 Hours	7 Days
4	Negative	Negative	Negative	10^3	10^3
5	Negative	Negative	Negative	10^3	10^3
6	Negative	Negative	Negative	10^3	10^3

* Initial inoculum is 10^6 for all tests.

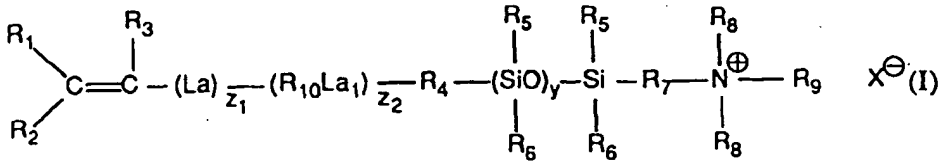
Example 7 illustrates a typical procedure for preparing contact lenses from the quaternary ammonium group-containing organosilicon monomers of the present invention.

Example 7 :

Contact lenses are prepared from the following formulation: 9.85 g 2-hydroxyethyl methacrylate, 0.05 g ethyleneglycol dimethacrylate, 0.10 g 3-methacryloxypropyltetramethyl-disiloxanylpropyldimethyloctadecylammonium chloride (MADAC) and 0.05 g 2-hydroxy-2-methyl-1-phenyl-propan-1-one. The formulation is stirred to effect solution and cured via actinic irradiation. After a two-hour cure, the resulting lenses are clear and colorless.

Claims

1. An antimicrobial quaternary ammonium group-containing polymer comprising in its structure repeating monomer units of the formula I



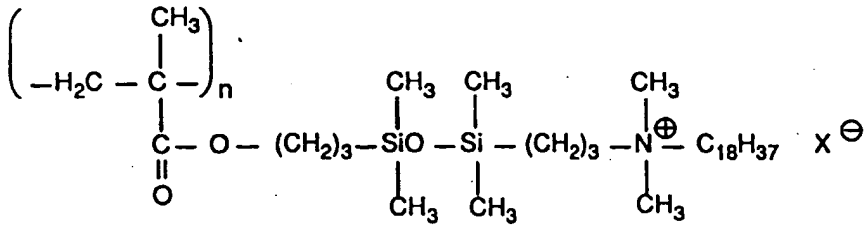
wherein R_1, R_2 and R_3 are independently hydrogen, C_1-C_7 alkyl, or -$COOR_{13}$ with R_{13} being hydrogen or C_1-C_4 alkyl;
z_1 and z_2 are independently 0 or 1;
La is -C(O)O-, -C(O)N(R_a)-, or a bond;
La_1 is a bond, -C(O)O-, -C(O)N(R_a)-, -O-, -OC(O)O-, -N(R_a)C(O)N(R_a)- or -N(R_a)C(O)O-; wherein R_a is hydrogen or C_1-C_8 alkyl;
R_{10} is a bivalent C_1-C_{20} aliphatic, C_3-C_{25} cycloaliphatic or C_6-C_{20} aryl group, each of which may be substituted with up to five halogen atoms, or $(CH_2CH(R_a)O)_j$, wherein j is an integer from 1 to 50;
R_4 and R_7 are independently a bivalent group selected from C_2-C_{10} aliphatic, such as C_2-C_8 alkylen , C_1-C_4 alkylen -(oxy-C_1-C_4 alkylene)$_g$, C_1-C_4 alkylene-OCH_2-(hydroxy C_1-C_4 alkylene)-CH_2, cycloaliphatic up to 25 carbon atoms and aryl up to 25 carbon atoms, wherein g is an integer from 1 to 10;
y is an integer from 1 to 10;
R_5 and R_6 are independently C_1-C_8 alkyl, C_6-C_{25} aryl, or C_6-C_{25} cycloaliphatic which may be substituted by

on or more halogen, hydroxy, C_1-C_4 alkyl, carboxy or C_1-C_{12} perhaloalkyl groups, or R_5 and R_6 may be -Si $(OSiCH_3)_3$;
R_8 and R_9 are independently C_1-C_{24} alkyl, C_3-C_{24} cycloaliphatic or C_6-C_{25} aryl, which groups may be each substituted with from 1 to 11 groups selected from hydroxy, C_1-C_4 alkyl, carboxy, C_1-C_{12} perhaloalkyl, and halogen, or R_8 and R_9 may also b $(CH_2CH_2O)_xH$ units, where x is an integer from 1 to 10, and
X is an ophthalmically acceptable counterion.

2. An antimicrobial quaternary ammonium group-containing polymer according to claim 1 in which the counterion X is selected from the group consisting of halogen, hydroxyl, acetate, SO_4^{2-}, CO_3^{2-} and PO_4^{3-}.

3. An antimicrobial quaternary ammonium group-containing polymer according to claim 1 in which the polymer is a homopolymer containing repeating monomer units of the formula I.

4. An antimicrobial quaternary ammonium group-containing homopolymer according to claim 3 of the formula



wherein n is an integer of 10 to about 3000 and X is an ophthalmically acceptable counterion.

5. An antimicrobial quaternary ammonium group-containing homopolymer according to claim 4 in which X is Cl.

6. An antimicrobial quaternary ammonium group-containing polymer according to claim 1 in which the polymer is a copolymer of a monomer of formula I and at least one suitable comonomer.

7. An antimicrobial quaternary ammonium group-containing polymer according to claim 6 in which the comonomer is selected from the group consisting of vinyl aromatics, lower alkenes having up to seven carbon atoms, lower alkadienes having up to seven carbon atoms, vinyl acetamide, vinyl amines, vinyl acetate, vinyl alcohols, acrylic acid, acrylate and methacrylate esters, acrylamides, N-vinylpyridine and derivatives thereof, N-vinylpyrrolidone and derivatives thereof, and vinyl benzyl ethers of polyethylene glycols and their monoalkyl ethers.

8. An antimicrobial quaternary ammonium group-containing polymer according to claim 1 in which the polymer is crosslinked with a suitable crosslinking agent.

9. An antimicrobial quaternary ammonium group-containing polymer according to claim 1 in which the polymer has a weight average molecular weight of 2000 to about 1000000.

10. A liquid composition comprising a solvent and an antimicrobially effective amount of the antimicrobial quaternary ammonium group-containing polymer of claim 1.

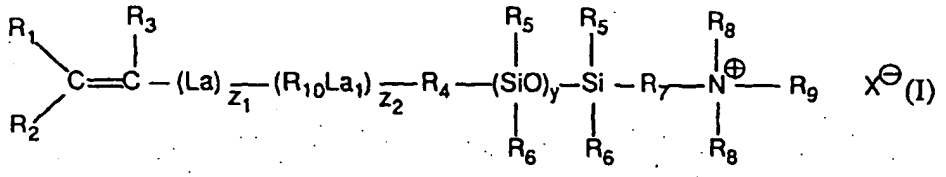
11. A liquid composition according to claim 10 in which the solvent is water.

12. An aqueous ophthalmic solution comprising an antimicrobially effective amount of the antimicrobial quaternary ammonium group-containing polymer of claim 1.

13. A method for cl aning and disinfecting contact lenses which comprises treating the contact lenses with an aqueous solution containing an antimicrobially ffective amount of the antimicrobial quaternary ammonium group-containing polymer according to claim 1.

14. A contact lens made from the antimicrobial polym r of any one of claims 1, 3, 6 or 8.

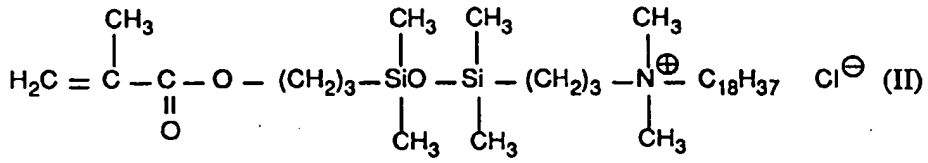
15. An antimicrobial quaternary ammonium group-containing monomer of the formula I:



(I)

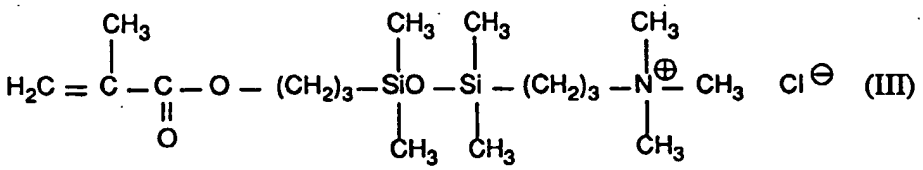
wherein R_1, R_2 and R_3 are independently hydrogen, C_1-C_7 alkyl, or -$COOR_{13}$ with R_{13} being hydrogen or C_1-C_4 alkyl;
z_1 and z_2 are independently 0 or 1;
La is -C(O)O-, -C(O)N(R_a)-, or a bond;
La_1 is a bond, -C(O)O-, -C(O)N(R_a)-, -O-, -OC(O)O-, -N(R_a)C(O)N(R_a)- or -N(R_a)C(O)O-; wherein R_a is hydrogen or C_1-C_8 alkyl;
R_{10} is a bivalent C_1-C_{20} aliphatic, C_3-C_{25} cycloaliphatic or C_6-C_{20} aryl group, each of which may be substituted with up to five halogen atoms, or $(CH_2CH(R_a)O)_j$, wherein j is an integer from 1 to 50;
R_4 and R_7 are independently a bivalent group selected from C_2-C_{10} aliphatic, such as C_2-C_8 alkylene, C_1-C_4 alkylene-(oxy-C_1-C_4 alkylene)g, C_1-C_4 alkylene-OCH_2-(hydroxy C_1-C_4 alkylene)-CH_2, cycloaliphatic up to 25 carbon atoms and aryl up to 25 carbon atoms, wherein g is an integer from 1 to 10;
y is an integer from 1 to 10;
R_5 and R_6 are independently C_1-C_8 alkyl, C_6-C_{25} aryl, or C_6-C_{25} cycloaliphatic which may be substituted by one or more halogen, hydroxy, C_1-C_4 alkyl, carboxy or C_1-C_{12} perhaloalkyl groups, or R_5 and R_6 may be -Si$(OSiCH_3)_3$;
R_8 and R_9 are independently C_1-C_{24} alkyl, C_3-C_{24} cycloaliphatic or C_6-C_{25} aryl, which groups may be each substituted with from 1 to 11 groups selected from hydroxy, C_1-C_4 alkyl, carboxy, C_1-C_{12} perhaloalkyl, and halogen, or R_8 and R_9 may also be $(CH_2CH_2O)_xH$ units, where x is an integer from 1 to 10, and
X is an ophthalmically acceptable counterion.

16. An antimicrobial monomer according to claim 15 of the formula II



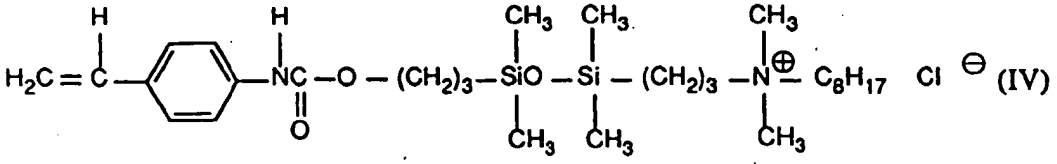
(II)

17. An antimicrobial monomer according to claim 15 of the formula III

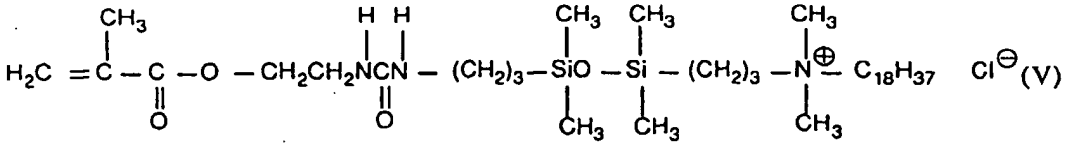


(III)

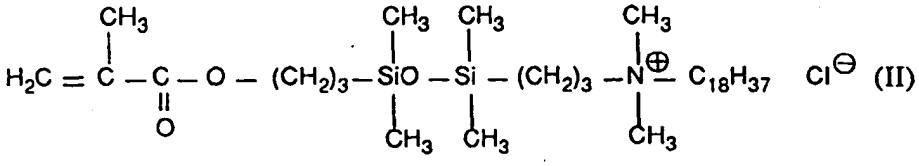
18. An antimicrobial monomer according to claim 15 of the formula IV



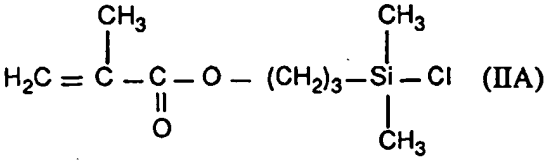
19. An antimicrobial monomer according to claim 15 of the formula V



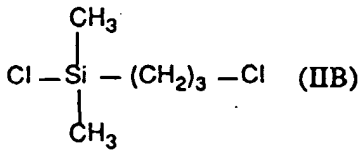
20. A method of producing an antimicrobial monomer of the formula II



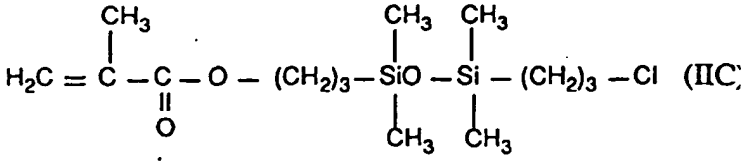
by (1) reacting a compound of the formula IIA



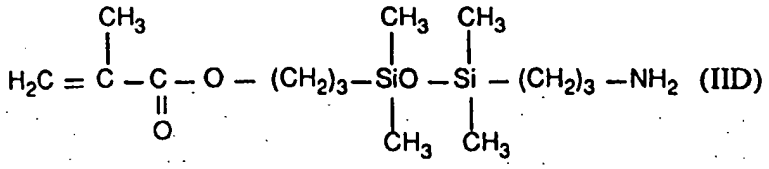
with a compound of the formula IIB



in the presence of water to produce a compound of the formula IIC

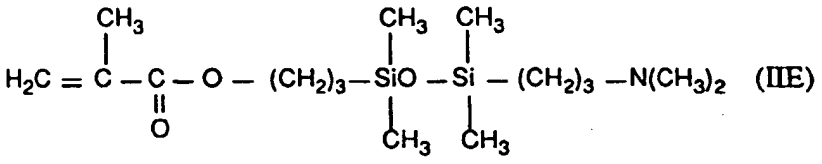


(2) reacting the compound of the formula (IIC) with an excess of NH_3, to produce a compound of the formula IID



(IID)

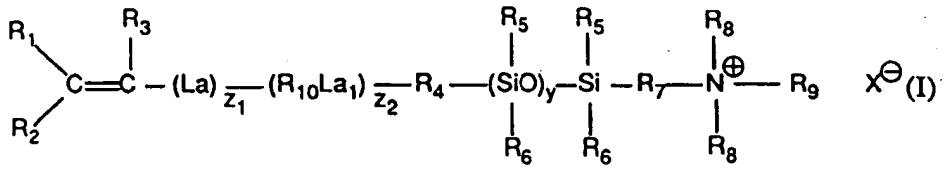
(3) reacting said compound of the formula IID with an excess of CH_3Br to produce a compound of the formula IIE



(IIE)

and (4) quaternizing the compound of the formula IIE with $C_{18}H_{37}Cl$ to produce a compound of formula II.

21. A method of producing an antimicrobial quaternary ammonium group-containing polymer which comprises homopolymerizing or copolymerizing, with a suitable comonomer, an antimicrobial monomer of the formula I

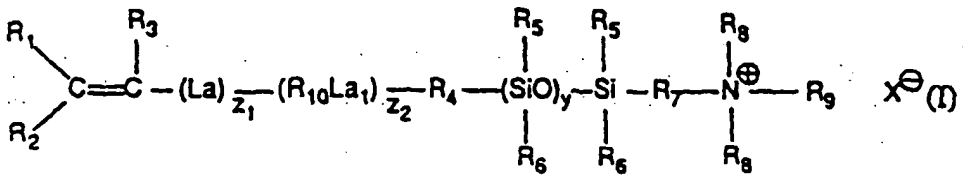


(I)

wherein R_1, R_2 and R_3 are independently hydrogen, C_1-C_7 alkyl, or $-COOR_{13}$ with R_{13} being hydrogen or C_1-C_4 alkyl;
z_1 and z_2 are independently 0 or 1;
La is $-C(O)O-$, $-C(O)N(R_a)-$, or a bond;
La_1 is a bond, $-C(O)O-$, $-C(O)N(R_a)-$, $-O-$, $-OC(O)O-$, $-N(R_a)C(O)N(R_a)-$ or $-N(R_a)C(O)O-$; wherein R_a is hydrogen or C_1-C_8 alkyl;
R_{10} is a bivalent C_1-C_{20} aliphatic, C_3-C_{25} cycloaliphatic or C_6-C_{20} aryl group, each of which may be substituted with up to five halogen atoms, or $(CH_2CH(R_a)O)_j$, wherein j is an integer from 1 to 50;
R_4 and R_7 are independently a bivalent group selected from C_2-C_{10} aliphatic, such as C_2-C_8 alkylene, C_1-C_4 alkylene-(oxy-C_1-C_4 alkylene)$_g$, C_1-C_4 alkylene-OCH_2-(hydroxy C_1-C_4 alkylene)-CH_2, cycloaliphatic up to 25 carbon atoms and aryl up to 25 carbon atoms, wherein g is an integer from 1 to 10;
y is an integer from 1 to 10;
R_5 and R_6 are independently C_1-C_8 alkyl, C_6-C_{25} aryl, or C_6-C_{25} cycloaliphatic which may be substituted by one or more halogen, hydroxy, C_1-C_4 alkyl, carboxy or C_1-C_{12} perhaloalkyl groups, or R_5 and R_6 may be $-Si(OSiCH_3)_3$;
R_8 and R_9 are independently C_1-C_{24} alkyl, C_3-C_{24} cycloaliphatic or C_6-C_{25} aryl, which groups may be each substituted with from 1 to 11 groups selected from hydroxy, C_1-C_4 alkyl, carboxy, C_1-C_{12} perhaloalkyl, and halogen, or R_8 and R_9 may also be $(CH_2CH_2O)_xH$ units, where x is an integer from 1 to 10, and
X is an ophthalmically acceptable counterion.

Pat ntansprüch

1. Antimikrobi lles, quaternäre Ammoniumgruppen enthaltendes Polymer, umfassend in seiner Struktur sich wiederholende Monomereinheiten der Formel I

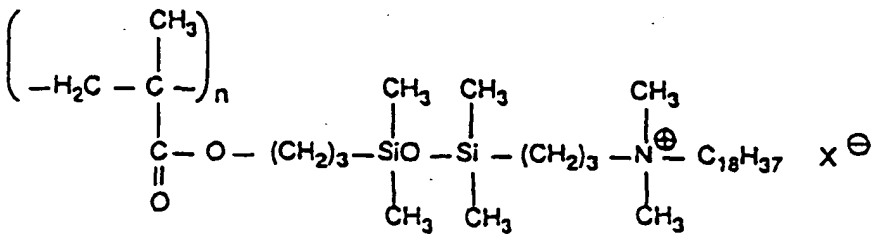


worin R_1, R_2 und R_3, unabhängig voneinander, Wasserstoff, C_1-C_7-Alkyl oder -$COOR_{13}$ darstellen, wobei R_{13} Wasserstoff oder C_1-C_4-Alkyl bedeutet;
z_1 und z_2 unabhängig 0 oder 1 sind;
La -C(O)O-, -C(O)N(R_a)- oder eine Bindung darstellt;
La_1 eine Bindung, -C(O)O-, -c(o)N(R_a)-, -O-, -OC(O)O-, -N(R_a)C(O)N(R_a)- oder -N(R_a)C(O)O- darstellt, worin R_a Wasserstoff oder C_1-C_8-Alkyl darstellt;
R_{10} eine zweiwertige aliphatische C_1-C_{20}-, cycloaliphatische C_3-C_{25}- oder C_6-C_{20}-Aryl-Gruppe, wobei jede davon mit bis zu fünf Halogenatomen substituiert sein kann, oder $(CH_2CH(R_a)O)_j$ darstellt, worin j eine ganze Zahl von 1 bis 50 ist;
R_4 und R_7, unabhängig voneinander, eine zweiwertige Gruppe, ausgewählt aus aliphatischen C_2-C_{10}-Gruppen, wie C_2-C_8-Alkylen, C_1-C_4-Alkylen-(oxy-C_1-C_4-alkylen)$_g$-, C_1-C_4-Alkylen-OCH_2-(hydroxy-C_1-C_4-alkylen) -CH_2-, cycloaliphatischen Gruppen mit bis zu 25 Kohlenstoffatomen und Arylgruppen mit bis zu 25 Kohlenstoffatomen, worin g eine ganze Zahl von 1 bis 10 ist, darstellen;
y eine ganze Zahl von 1 bis 10 ist;
R_5 und R_6, unabhängig voneinander, eine C_1-C_8-Alkyl-, C_6-C_{25}-Aryl- oder cycloaliphatische C_6-C_{25}-Gruppe bedeuten, die mit ein oder mehreren Halogen-, Hydroxy-, C_1-C_4-Alkyl-, Carboxy- oder C_1-C_{12}-Perhalogenalkylgruppen substituiert sein können oder R_5 und R_6 -Si($OSiCH_3$)$_3$ sein können;
R_8 und R_9, unabhängig voneinander, eine C_1-C_{24}-Alkyl-, cycloaliphatische C_3-C_{24}- oder C_6-C_{25}-Aryl-Gruppe darstellen, wobei die Gruppen jeweils mit 1 bis 11 Gruppen, ausgewählt aus Hydroxy, C_1-C_4-Alkyl, Carboxy, C_1-C_{12}-PerhaPogen-alkyl und Halogen substituiert sein können oder R_8 und R_9 ebenfalls $(CH_2CH_2O)_xH$-Einheiten sein können, wobei x eine ganze Zahl von 1 bis 10 ist und
X ein ophthalmisch verträgliches Gegenion darstellt.

2. Antimikrobielles, quaternäre Ammoniumgruppen enthaltendes Polymer nach Anspruch 1, worin das Gegenion X ausgewählt ist aus der Gruppe, bestehend aus Halogen, Hydroxyl, Acetat, SO_4^{2-}, CO_3^{2-} und PO_4^{3-}.

3. Antimikrobielles, quaternäre Ammoniumgruppen enthaltendes Polymer nach Anspruch 1, worin das Polymer ein Homopolymer ist, das sich wiederholende Monomereinheiten der Formel I enthält.

4. Antimikrobielles, quaternäre Ammoniumgruppen enthaltendes Homopolymer nach Anspruch 3 der Formel



worin n eine ganze Zahl von 10 bis etwa 3000 ist und X ein ophthalmisch verträgliches Gegenion darstellt.

5. Antimikrobielles, quat märe Ammoniumgruppen enthaltendes Homopolymer nach Anspruch 4, worin X Cl darstellt.

6. Antimikrobielles, quaternäre Ammoniumgruppen enthaltendes Polymer nach Anspruch 1, wobei das Polymer ein Copolymer aus einem Monomer der Formel I und mindestens einem geeigneten Comonomer ist.

7. Antimikrobielles, quaternäre Ammoniumgruppen enthaltendes Polymer nach Anspruch 6, wobei das Comonomer ausgewählt ist aus der Gruppe, bestehend aus Vinylaromaten, Niederalkenen mit bis zu sieben Kohlenstoffatomen, Niederalkadienen mit bis zu sieben Kohlenstoffatomen, Vinylacetamid, Vinylaminen, Vinylacetat, Vinylalkoholen, Acrylsäure, Acrylat-und Methacrylatestern, Acrylamiden, N-Vinylpyridin und Derivaten davon, N-Vinylpyrrolidon und Derivaten davon und Vinylbenzylethern von Polyethylenglycolen und deren Monoalkylethern.

8. Antimikrobielles, quaternäre Ammoniumgruppen enthaltendes Polymer nach Anspruch 1, wobei das Polymer mit einem geeigneten Vernetzungsmittel vernetzt ist.

9. Antimikrobielles, quaternäre Ammoniumgruppen enthaltendes Polymer nach Anspruch 1, wobei das Polymer ein gewichtsmittleres Molekulargewicht von 2000 bis etwa 1 000 000 aufweist.

10. Flüssige Zusammensetzung, umfassend ein Lösungsmittel und eine antimikrobiell wirksame Menge des antimikrobiellen, quaternäre Ammoniumgruppen enthaltenden Polymers von Anspruch 1.

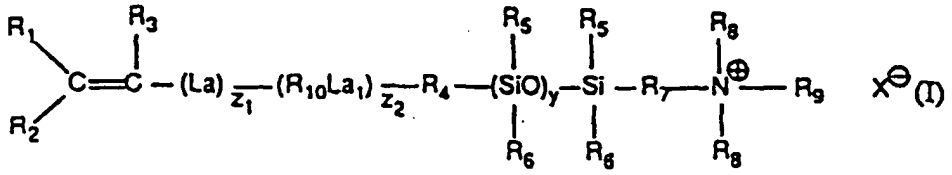
11. Flüssige Zusammensetzung nach Anspruch 10, wobei das Lösungsmittel Wasser darstellt.

12. Wässerige ophthalmische Lösung, umfassend eine antimikrobiell wirksame Menge des antimikrobiellen, quaternäre Ammoniumgruppen enthaltenden Polymers von Anspruch 1.

13. Verfahren zur Reinigung und Desinfizierung von Kontaktlinsen, umfassend Behandeln der Kontaktlinsen mit einer wässerigen Lösung, enthaltend eine antimikrobiell wirksame Menge des antimikrobiellen, quaternäre Ammoniumgruppen enthaltenden Polymers nach Anspruch 1.

14. Kontaktlinsen, hergestellt aus dem antimikrobiellen Polymer nach einem der Ansprüche 1, 3, 6 oder 8.

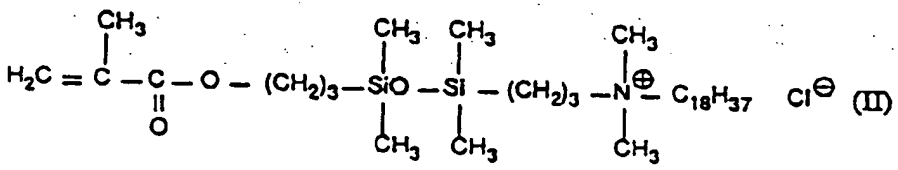
15. Antimikrobielles, quaternäre Ammoniumgruppen enthaltendes Monomer der Formel I:



worin R_1, R_2 und R_3, unabhängig voneinander, Wasserstoff, C_1-C_7-Alkyl oder -$COOR_{13}$ darstellen, wobei R_{13} Wasserstoff oder C_1-C_4-Alkyl bedeutet;
z_1 und z_2 unabhängig 0 oder 1 sind;
La -C(O)O-, -C(O)N(R_a)- oder eine Bindung darstellt;
La_1 eine Bindung, -C(O)O-, -C(O)N(R_a)-, -O-, -OC(O)O-, -N(R_a)C(O)N(R_a)- oder -N(R_a)C(O)O- darstellt, worin R_a Wasserstoff oder C_1-C_8-Alkyl darstellt;
R_{10} eine zweiwertige aliphatische C_1-C_{20}-, cycloaliphatische C_3-C_{25}- oder C_6-C_{20}-Aryl-Gruppe, wobei jede davon mit bis zu fünf Halogenatomen substituiert sein kann, oder $(CH_2CH(R_a)O)_j$ darstellt, worin j eine ganze Zahl von 1 bis 50 ist;
R_4 und R_7, unabhängig voneinander, eine zweiwertige Gruppe, ausgewählt aus aliphatischen C_2-C_{10}-Gruppen, wie C_2-C_8-Alkylen, C_1-C_4-Alkylen-(oxy-C_1-C_4-alkylen)$_g$-, C_1-C_4-Alkylen-OCH_2-(hydroxy-C_1-C_4-alkylen)-CH_2-, cycloaliphatischen Gruppen mit bis zu 25 Kohlenstoffatomen und Arylgruppen mit bis zu 25 Kohlenstoffatomen, worin g eine ganze Zahl von 1 bis 10 ist, darstellen;
y eine ganze Zahl von 1 bis 10 ist;
R_5 und R_6, unabhängig voneinander, in C_1-C_8-Alkyl-, C_6-C_{25}-Aryl- oder cycloaliphatische C_6-C_{25}-Gruppe bedeuten, die mit ein oder mehrern Halogen-, Hydroxy-, C_1-C_4-Alkyl-, Carboxy- oder C_1-C_{12}-Perhalogenalkylgruppen substituiert sein können oder R_5 und R_6 -Si($OSiCH_3$)$_3$ sein können;
R_8 und R_9, unabhängig voneinander, eine C_1-C_{24}-Alkyl-, cycloaliphatisch C_3-C_{24}- oder C_6-C_{25}-Aryl-Gruppe darstellen, wobei die Gruppen jeweils mit 1 bis 11 Gruppen, ausgewählt aus Hydroxy, C_1-C_4-Alkyl, Carboxy,

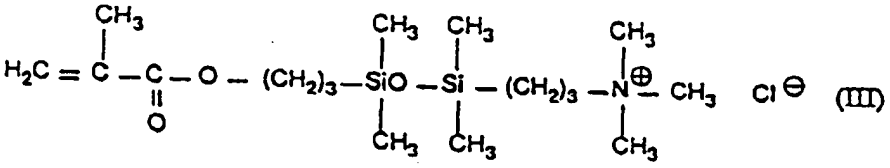
C_1-C_{12}-Perhalogen-alkyl und Halogen substituiert sein können oder R_8 und R_9 ebenfalls $(CH_2CH_2O)_xH$-Einheiten sein können, wobei x eine ganze Zahl von 1 bis 10 ist und
X ein ophthalmisch verträgliches Gegenion darstellt.

16. Antimikrobielles Monomer nach Anspruch 15 der Formel II



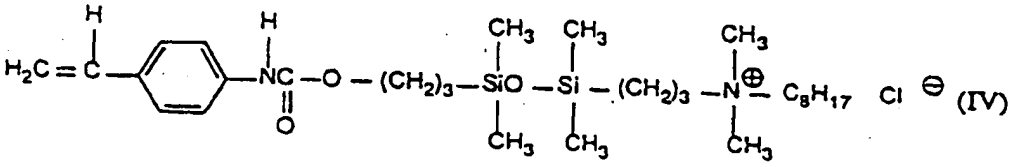
(II)

17. Antimikrobielles Monomer nach Anspruch 15 der Formel III



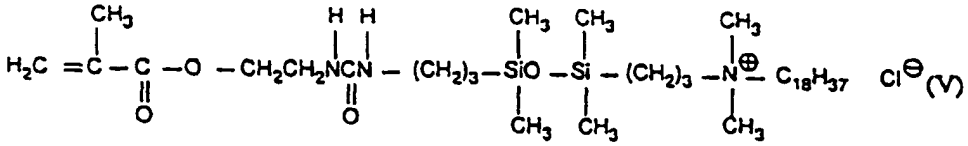
(III)

18. Antimikrobielles Monomer nach Anspruch 15 der Formel IV



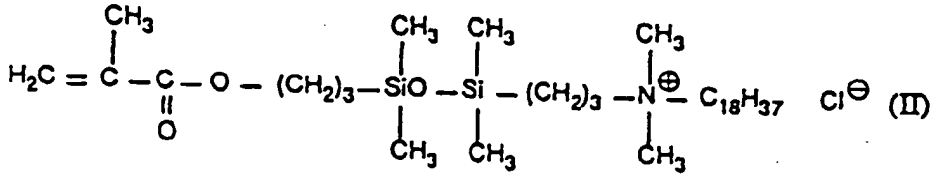
(IV)

19. Antimikrobielles Monomer nach Anspruch 15 der Formel V



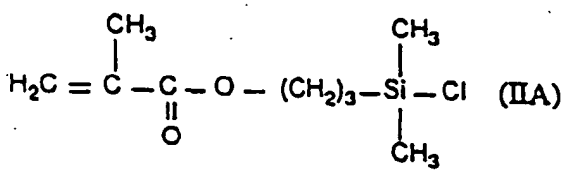
(V)

20. Verfahren zur Herstellung eines antimikrobiellen Monomers der Formel II



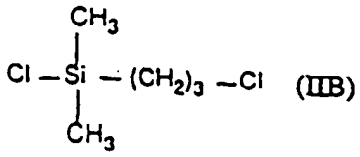
(II)

durch (1) Umsetzen iner Verbindung der Formel IIA



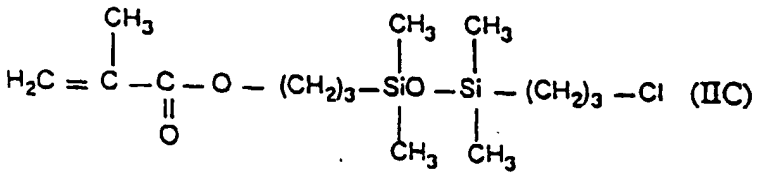
(IIA)

mit einer Verbindung der Formel IIB



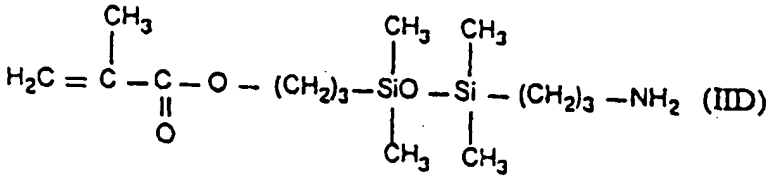
(IIB)

in Gegenwart von Wasser zur Herstellung einer Verbindung der Formel IIC



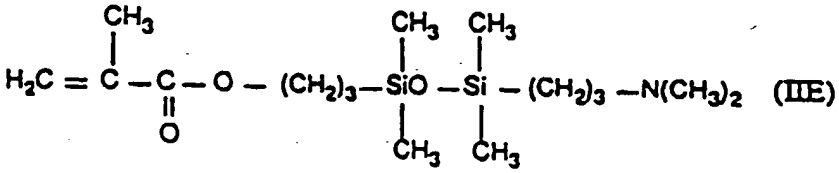
(IIC)

(2) Umsetzen der Verbindung der Formel (IIC) mit einem Überschuß an NH_3, zur Herstellung einer Verbindung der Formel IID



(IID)

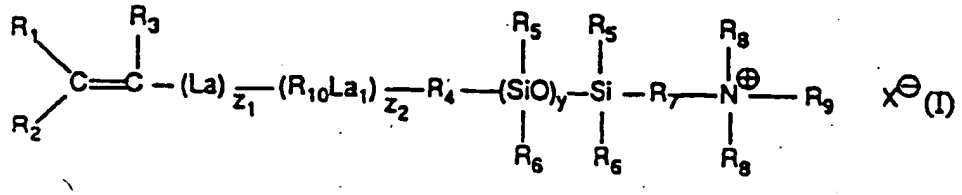
(3) Umsetzen der Verbindung der Formel IID mit einem Überschuß an CH_3Br zur Herstellung einer Verbindung der Formel IIE



(IIE)

und (4) Quaternisieren der Verbindung der Formel IIE mit $C_{18}H_{37}Cl$ zur Herstellung einer Verbindung der Formel II.

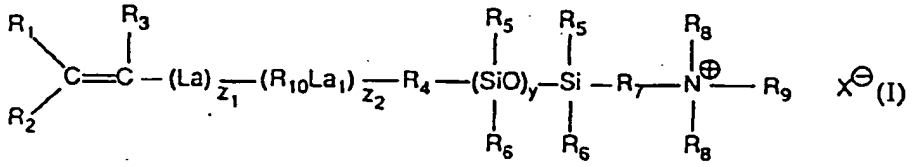
21. Verfahren zur Herstellung eines antimikrobiellen, quaternäre Ammoniumgruppen enthaltenden Polym rs, umfassend Homopolymerisi ren oder Copolymerisieren mit einem geeigneten comonomer, ein s antimikrobiellen Monomers der Formel I



worin R_1, R_2 und R_3, unabhängig voneinander, Wasserstoff, C_1-C_7-Alkyl oder -$COOR_{13}$ darstellen, wobei R_{13} Wasserstoff oder C_1-C_4-Alkyl bedeutet;
z_1 und z_2 unabhängig 0 oder 1 sind;
La -C(O)O-, -C(O) N (R_a) - oder eine Bindung darstellt;
La_1 eine Bindung, -C(O)O-, -C(O)N(R_a)-, -O-, -OC(O)O-, -N(R_a)C(O)N(R_a)- oder -N(R_a)C(O)O- darstellt, worin R_a Wasserstoff oder C_1-C_8-Alkyl darstellt;
R_{10} eine zweiwertige aliphatische C_1-C_{20}-, cycloaliphatische C_3-C_{25}- oder C_6-C_{20}-Aryl-Gruppe, wobei jede davon mit bis zu fünf Halogenatomen substituiert sein kann, oder $(CH_2CH(R_a)O)_j$ darstellt, worin j eine ganze Zahl von 1 bis 50 ist;
R_4 und R_7, unabhängig voneinander, eine zweiwertige Gruppe, ausgewählt aus aliphatischen C_2-C_{10}-Gruppen, wie C_2-C_8-Alkylen, C_1-C_4-Alkylen- (oxy-C_1-C_4-alkylen)$_g$-, C_1-C_4-Alkylen-OCH_2-(hydroxy-C_1-C_4-alkylen) -CH_2-, cycloaliphatischen Gruppen mit bis zu 25 Kohlenstoffatomen und Arylgruppen mit bis zu 25 Kohlenstoffatomen, worin g eine ganze Zahl von 1 bis 10 ist, darstellen;
y eine ganze Zahl von 1 bis 10 ist;
R_5 und R_6, unabhängig voneinander, eine C_1-C_8-Alkyl-, C_6-C_{25}-Aryl- oder cycloaliphatische C_6-C_{25}-Gruppe bedeuten, die mit ein oder mehreren Halogen-, Hydroxy-, C_1-C_4-Alkyl-, Carboxy- oder C_1-C_{12}-Perhalogenalkylgruppen substituiert sein können oder R_5 und R_6 -Si($OSiCH_3$)$_3$ sein können;
R_8 und R_9, unabhängig voneinander, eine C_1-C_{24}-Alkyl-, cycloaliphatische C_3-C_{24}- oder C_6-C_{25}-Aryl-Gruppe darstellen, wobei die Gruppen jeweils mit 1 bis 11 Gruppen, ausgewählt aus Hydroxy, C_1-C_4-Alkyl, Carboxy, C_1-C_{12}-Perhalogen-alkyl und Halogen substituiert sein können oder R_8 und R_9 ebenfalls $(CH_2CH_2O)_xH$-Einheiten sein können, wobei x eine ganze Zahl von 1 bis 10 ist und
X ein ophthalmisch verträgliches Gegenion darstellt.

Revendications

1. Polymère antimicrobien contenant des groupes ammonium quaternaire, comprenant, dans sa structure, des motifs monomères récurrents de formule I



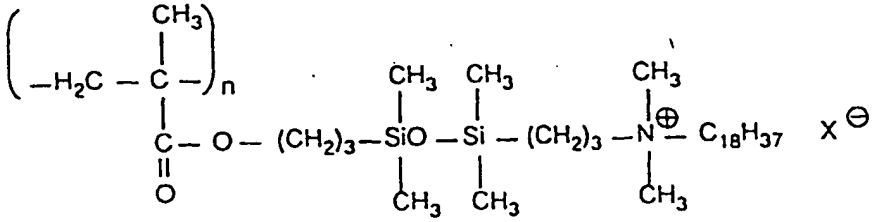
dans laquelle R_1, R_2 et R_3 sont, indépendamment, des atomes d'hydrogène ou des groupes alkyle en C_1-C_7 ou -$COOR_{13}$, R_{13} étant un atome d'hydrogène ou un groupe alkyle en C_1-C_4; Z_1 et Z_2 sont indépendamment 0 ou 1;
La est-C(O)O-, -C(O)N(R_a)-, ou une liaison;
La_1 est une liaison, -C(O)O-, -C(O)N(R_a)-, -O-, -OC(O)O-, -N(R_a)C(O)N(R_a)- ou -N(R_a)C(O)O-; où R_a est un atome d'hydrogène ou un groupe alkyle en C_1-C_8;
R_{10} est un groupe aliphatique en C_1-C_{20}, cycloaliphatique en C_3-C_{25} ou aryle en C_6-C_{20}, bivalent, chacun pouvant être substitué par jusqu'à 5 atomes d'halogène, ou bien $(CH_2CH(R_a)O)_j$, où j est un nombre entier de 1 à 50;
R_4 et R_7 sont, indépendamment, des group s bivalents choisis parmi les groupes aliphatiques n C_2-C_{10}, tels que alkylène en C_2-C_8, (alkylène en C_1-C_4)-(oxy-alkylèn n C_1-C_4)$_g$, (alkylène en C_1-C_4)-OCH_2-(hydroxyalkylène en C_1-C_4)-CH_2, des groupes cycloaliphatiqu s contenant jusqu'à 25 atomes de carbone et des groupes aryle contenant jusqu'à 25 atomes de carbon , où g est un nombre ntier de 1 à 10;

y st un nombr entier de 1 à 10;
R_5 et R_6 sont, indépendamment, des groupes alkyle en C_1-C_8, aryle en C_6-C_{25} ou cycloaliphatiques en C_6-C_{25} qui peuvent être substitués par un ou plusieurs groupes halogéno, hydroxy, alkyle en C_1-C_4, carboxy ou perhalogénoalkyl n C_1-C_{12}, ou bien R_5 et R_6 peuvent être -Si(OSiCH_3)$_3$;
R_8 et R_9 sont, indépendamment, des group s alkyle en C_1-C_{24}, cycloaliphatiques en C_3-C_{24} ou aryle en C_6-C_{25}, qui peuv nt ˆtre substitués chacun par 1 à 11 groupes choisis parmi les groupes hydroxy, alkyle en C_1-C_4, carboxy, perhalogénoalkyle en C_1-C_{12} et halogéno, ou bien R_8 et R_9 peuvent être aussi des motifs $(CH_2CH_2O)_xH$, où x est un nombre entier de 1 à 10, et
X est un contre-ion acceptable en ophtalmologie.

2. Polymère antimicrobien contenant des groupes ammonium quaternaire selon la revendication 1, dans lequel le contre-ion X est choisi dans le groupe constitué par les groupes halogéno, hydroxyle, acétate, SO_4^{2-}, CO_3^{2-} et PO_4^{3-}.

3. Polymère antimicrobien contenant des groupes ammonium quaternaire selon la revendication 1, dans lequel le polymère est un homopolymère contenant des motifs monomères récurrents de formule I.

4. Homopolymère antimicrobien contenant des groupes ammonium quaternaire selon la revendication 3, de formule



dans laquelle n est un nombre entier de 10 à environ 3 000 et X est un contre-ion acceptable en ophtalmologie.

5. Homopolymère antimicrobien contenant des groupes ammonium quaternaire selon la revendication 4, dans lequel X est Cl.

6. Polymère antimicrobien contenant des groupes ammonium quaternaire selon la revendication 1, dans lequel le polymère est un copolymère d'un monomère de formule I et d'au moins un comonomère convenable.

7. Polymère antimicrobien contenant des groupes ammonium quaternaire selon la revendication 6, dans lequel le comonomère est choisi dans le groupe constitué par les vinylaromatiques, les alcènes inférieurs possédant jusqu'à 7 atomes de carbone, les alcadiènes inférieurs possédant jusqu'à 7 atomes de carbone, le vinylacétamide, les vinylamines, l'acétate de vinyle, les alcools vinyliques, l'acide acrylique, les esters acrylates et méthacrylates, les acrylamides, la N-vinylpyridine et ses dérivés, la N-vinylpyrrolidone et ses dérivés, et les vinylbenzyléthers de polyéthylèneglycols et leurs éthers monoalkyliques.

8. Polymère antimicrobien contenant des groupes ammonium quaternaire selon la revendication 1, dans lequel le polymère est réticulé avec un agent de réticulation convenable.

9. Polymère antimicrobien contenant des groupes ammonium quaternaire selon la revendication 1, dans lequel le polymère possède une masse moléculaire moyenne en poids de 2 000 à environ 1 000 000.

10. Composition liquide comprenant un solvant et une quantité antimicrobienne efficace du polymère antimicrobien contenant des groupes ammonium quaternaire de la revendication 1.

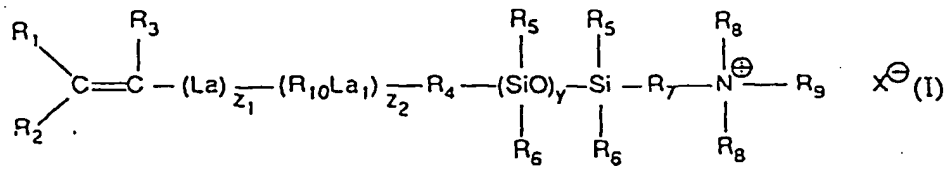
11. Composition liquide selon la revendication 10, dans laquell l solvant est de l'eau.

12. Solution aqueuse ophtalmique comprenant une quantité antimicrobienne efficac du polymère antimicrobien contenant des groupes ammonium quaternaire s lon la revendication 1.

13. Procédé pour nettoyer et désinfecter des lentilles de contact, qui consiste à traiter les lentilles de contact avec une solution aqueuse contenant une quantité antimicrobienne efficace du polymère antimicrobien contenant des groupes ammonium quaternaire selon la revendication 1.

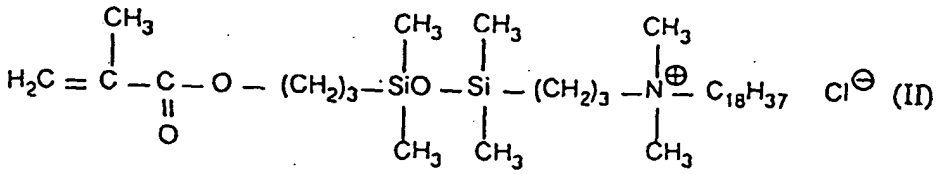
14. Lentilles de contact fabriquées à partir du polymère antimicrobien selon l'une quelconque des revendications 1, 3, 6 ou 8.

15. Monomère antimicrobien contenant des groupes ammonium quaternaire de formule I:

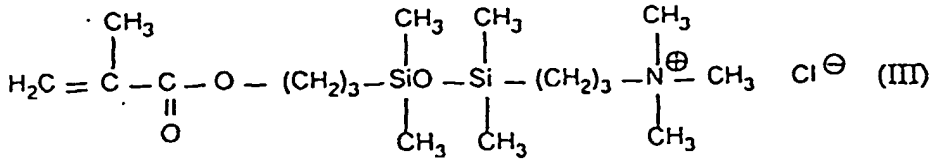


dans laquelle R_1, R_2 et R_3 sont, indépendamment, des atomes d'hydrogène ou des groupes alkyle en C_1-C_7 ou -$COOR_{13}$, R_{13} étant un atome d'hydrogène ou un groupe alkyle en C_1-C_4;
Z_1 et Z_2 sont indépendamment 0 ou 1;
La est -C(O)O-, -C(O)N(R_a)-, ou une liaison;
La_1 est une liaison, -C(O)O-, -C(O)N(R_a)-, -O-, -OC(O)O-, -N(R_a)C(O)N(R_a)- ou -N(R_a)C(O)O-; où R_a est un atome d'hydrogène ou un groupe alkyle en C_1-C_8;
R_{10} est un groupe aliphatique en C_1-C_{20}, cycloaliphatique en C_3-C_{25} ou aryle en C_6-C_{20}, bivalent, chacun pouvant être substitué par jusqu'à 5 atomes d'halogène, ou bien $(CH_2CH(R_a)O)_j$, où j est un nombre entier de 1 à 50;
R_4 et R_7 sont, indépendamment, des groupes bivalents choisis parmi les groupes aliphatiques en C_2-C_{10}, tels que alkylène en C_2-C_8, (alkylène en C_1-C_4)-(oxy-alkylène en C_1-C_4)$_g$, (alkylène en C_1-C_4)-OCH_2-(hydroxyalkylène en C_1-C_4)-CH_2, des groupes cycloaliphatiques contenant jusqu'à 25 atomes de carbone et des groupes aryle contenant jusqu'à 25 atomes de carbone, où g est un nombre entier de 1 à 10;
y est un nombre entier de 1 à 10;
R_5 et R_6 sont, indépendamment, des groupes alkyle en C_1-C_8, aryle en C_6-C_{25} ou cycloaliphatiques en C_6-C_{25} qui peuvent être substitués par un ou plusieurs groupes halogéno, hydroxy, alkyle en C_1-C_4, carboxy ou perhalogénoalkyle en C_1-C_{12}, ou bien R_5 et R_6 peuvent être -$Si(OSiCH_3)_3$;
R_8 et R_9 sont, indépendamment, des groupes alkyle en C_1-C_{24}, cycloaliphatiques en C_3-C_{24} ou aryle en C_6-C_{25}, qui peuvent être substitués chacun par 1 à 11 groupes choisis parmi les groupes hydroxy, alkyle en C_1-C_4, carboxy, perhalogénoalkyle en C_1-C_{12} et halogéno, ou bien R_8 et R_9 peuvent être aussi des motifs $(CH_2CH_2O)_xH$, où x est un nombre entier de 1 à 10, et
X est un contre-ion acceptable en ophtalmologie.

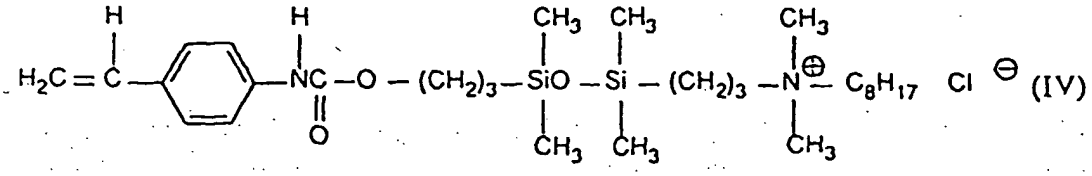
16. Monomère antimicrobien selon la revendication 15, de formule II



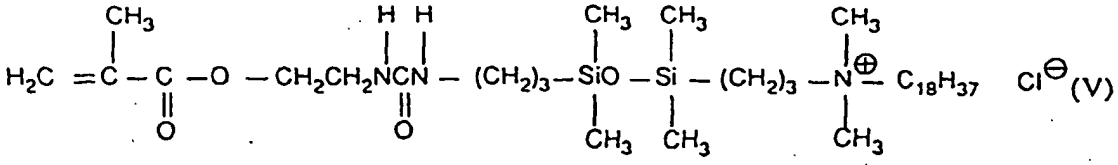
17. Monomère antimicrobien selon la revendication 15, de formule III



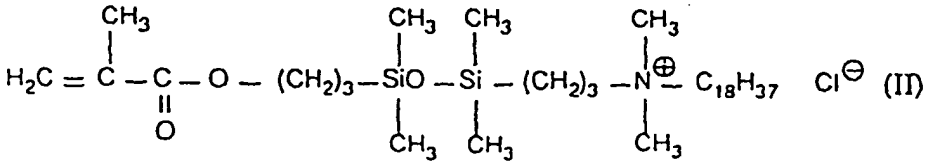
18. Monomèr antimicrobien selon la revendication 15, de formule IV



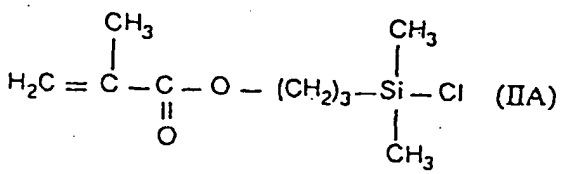
19. Monomère antimicrobien selon la revendication 15, de formule V



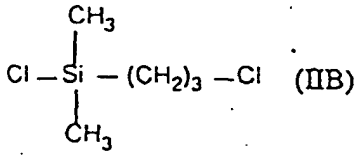
20. Procédé de production d'un monomère antimicrobien de formule II



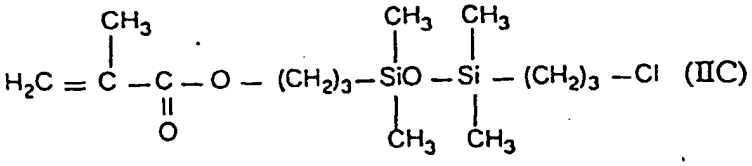
qui consiste à (1) faire réagir un composé de formule IIA



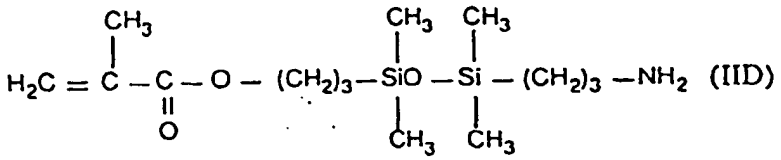
avec un composé de formule IIB



en présence d'eau, pour produire un composé de formule IIC

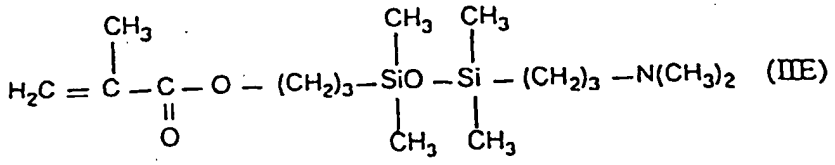


(2) faire réagir le composé de formule IIC avec un excès de NH_3, pour produire un composé de formul IID



(IID)

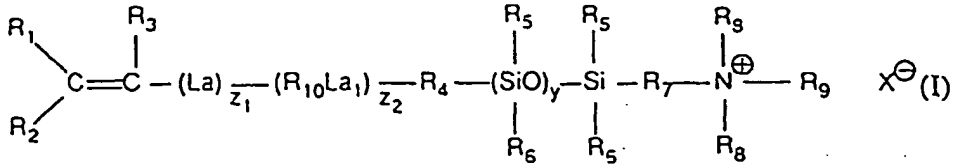
(3) faire réagir ledit composé de formule IID avec un excès de CH_3Br, pour produire un composé de formule IIE



(IIE)

et (4) quaterniser le composé de formule IIE avec $C_{18}H_{37}Cl$ pour produire un composé de formule II.

21. Procédé de production d'un polymère antimicrobien contenant des groupes ammonium quaternaire, qui comprend l'homopolymérisation ou la copolymérisation, avec un comonomère convenable, d'un monomère antimicrobien de formule I



(I)

dans laquelle R_1, R_2 et R_3 sont, indépendamment, des atomes d'hydrogène ou des groupes alkyle en C_1-C_7 ou $-COOR_{13}$, R_{13} étant un atome d'hydrogène ou un groupe alkyle en C_1-C_4;
Z_1 et Z_2 sont indépendamment 0 ou 1;
La est -C(O)O-, $-C(O)N(R_a)$-, ou une liaison;
La_1 est une liaison, -C(O)O-, $-C(O)N(R_a)$-, -O-, -OC(O)O-, $-N(R_a)C(O)N(R_a)$- ou $-N(R_a)C(O)O$-; où R_a est un atome d'hydrogène ou un groupe alkyle en C_1-C_8;
R_{10} est un groupe aliphatique en C_1-C_{20}, cycloaliphatique en C_3-C_{25} ou aryle en C_6-C_{20}, bivalent, chacun pouvant être substitué par jusqu'à 5 atomes d'halogène, ou bien $(CH_2CH(R_a)O)_j$, où j est un nombre entier de 1 à 50;
R_4 et R_7 sont, indépendamment, des groupes bivalents choisis parmi les groupes aliphatiques en C_2-C_{10}, tels que alkylène en C_2-C_8, (alkylène en C_1-C_4)-(oxy-alkylène en C_1-C_4)$_g$, (alkylène en C_1-C_4)-OCH_2-(hydroxyalkylène en C_1-C_4)-CH_2, des groupes cycloaliphatiques contenant jusqu'à 25 atomes de carbone et des groupes aryle contenant jusqu'à 25 atomes de carbone, où g est un nombre entier de 1 à 10;
y est un nombre entier de 1 à 10;
R_5 et R_6 sont, indépendamment, des groupes alkyle en C_1-C_8, aryle en C_6-C_{25} ou cycloaliphatiques en C_6-C_{25} qui peuvent être substitués par un ou plusieurs groupes halogéno, hydroxy, alkyle en C_1-C_4, carboxy ou perhalogénoalkyle en C_1-C_{12}, ou bien R_5 et R_6 peuvent être $-Si(OSiCH_3)_3$;
R_8 et R_9 sont, indépendamment, des groupes alkyle en C_1-C_{24}, cycloaliphatiques en C_3-C_{24} ou aryle en C_6-C_{25}, qui peuvent être substitués chacun par 1 à 11 groupes choisis parmi les groupes hydroxy, alkyle en C_1-C_4, carboxy, perhalogénoalkyle en C_1-C_{12} et halogéno, ou bien R_8 et R_9 peuvent être aussi des motifs $(CH_2CH_2O)_XH$, où x est un nombre entier de 1 à 10, et
X est un contre-ion acceptable en ophtalmologie.